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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,160	05/24/2007	Helge H. Rasmussen	U 016502-0	8069

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EXAMINER	
TOWNSLEY, SARA ELIZABETH	
ART UNIT	PAPER NUMBER
1613	

NOTIFICATION DATE	DELIVERY MODE
04/21/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/594,160	RASMUSSEN ET AL.	
	Examiner	Art Unit	
	SARA E. TOWNSLEY	1613	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-25* is/are pending in the application.

4a) Of the above claim(s) *1,2 and 15-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3 and 5-12* is/are rejected.

7)☒ Claim(s) *13 and 14* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL REJECTION

Receipt is acknowledged of Applicants' Amendments and Remarks, filed 11/30/2010.

Claim 4 has been cancelled.

Claims 3, 8, and 13 have been amended and incorporate no new matter.

Claims 1, 2, and 15-25 stand withdrawn as drawn to nonelected inventions and species.

No new claims have been added.

Thus, claims 3 and 5-14 now represent all claims currently pending and under consideration.

INFORMATION DISCLOSURE STATEMENT

No new Information Disclosure Statements (IDS) have been submitted.

WITHDRAWN REJECTIONS

Rejections under 35 USC §112

Due to the amendments to the claims, the rejection of claims 3 and 5-14 under 35 U.S.C. §112, second paragraph, for indefiniteness, has been withdrawn.

Due to the amendments to the claims, the rejection of claims 3 and 5-14 under 35 U.S.C. §112, first paragraph, for lack of written description, has been withdrawn.

Due to the amendments to the claims, the rejection of claims 3 and 5-14 under 35 U.S.C. §112, first paragraph, for lack of enablement, has been withdrawn.

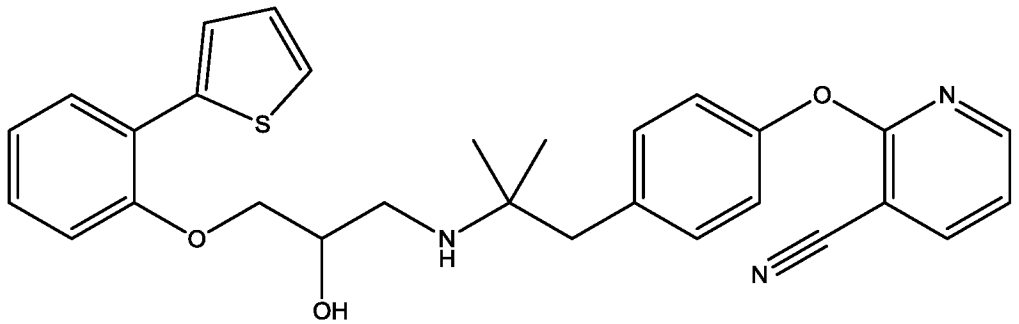
MAINTAINED REJECTIONS

The following rejections are maintained from the previous Office Action dated 9/1/2010, on the ground that the references cited therein continue to read on the limitations of the amended claims.

Claim Rejections - 35 USC § 102

Claims 3 and 5 stand rejected under 35 U.S.C. §102(b) as being anticipated by Bush et al. (WO02/94820).

Bush et al. disclose methods of administering a β_3 adrenoceptor agonist, in particular 2-(4-{2-[2-hydroxy-3-(2-thiophen-2-yl-phenoxy)-propylamino]-2-methyl-propyl}-phenoxy)-nicotinonitrile (SAM II),



2-(4-{2-[2-hydroxy-3-(2-thiophen-2-yl-phenoxy)-propylamino]-2-methyl-propyl}-phenoxy)-nicotinonitrile

to treat diseases in humans, including congestive heart failure (abstract; p. 25, lines 2-25), as recited by claim 3.

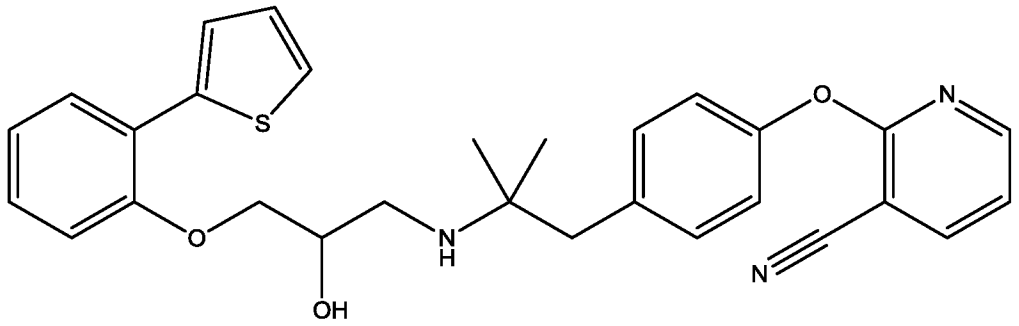
Because the core structure of SAM II is an aryloxypropanolamine, this compound falls within the scope of the term aryloxypropanolamine, as recited by claim 5.

Thus, Bush et al. anticipates claims 3 and 5.

Claim Rejections - 35 USC § 103

Claims 3 and 5-12 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Bush et al. (WO02/94820), in view of Moniotte et al. and the European Society of Cardiology (ESC) Guidelines.

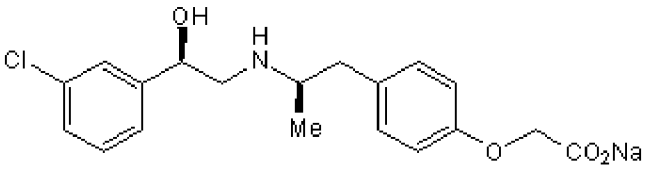
Bush et al. disclose methods of administering a β_3 adrenoceptor agonist, in particular 2-(4-{2-[2-hydroxy-3-(2-thiophen-2-yl-phenoxy)-propylamino]-2-methyl-propyl}-phenoxy)-nicotinonitrile (SAM II),



2-(4-{2-[2-hydroxy-3-(2-thiophen-2-yl-phenoxy)-propylamino]-2-methyl-propyl}-phenoxy)-nicotinonitrile

to treat diseases in humans, including congestive heart failure (abstract; p. 25, lines 2-25), as recited by claim 3.

Moniotte et al. disclose that BRL 37344, is a β_3-adrenoceptor agonist in human cardiac tissue (p. 485), as recited by claims 6 and 7. The structure of BRL 37344,



has an arylethanolamine core; thus, this compound falls within the scope of the term arylethanolamine, as recited by claim 5.

While Moniotte et al. does not explicitly disclose that BRL 37344 also has β_1- or β_2-adrenoceptor antagonist activity, as recited by claim 8, this is an inherent property of the compound. As recognized by MPEP §2112, the claiming of a new *property* which was inherently present in the prior art composition at all times does not distinguish it over the prior art. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430,433 (CCPA 1977). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.* 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003).

Moniotte et al. also disclose nadolol as a β_1-/β_2-adrenoceptor antagonist, and the simultaneous co-administration of BRL 37344 and nadolol (p. 485), as recited by claims 9-12. As disclosed by the **ESC Guidelines**, it was known in the art to administer β_1- and/or β_2-adrenoceptor antagonists (a.k.a. "β-blockers") as a pharmacological therapy to treat heart failure.

Because the references disclose the treatment of heart failure in humans by administering a β_3 adrenoceptor agonist, and/or a β_1-/β_2-adrenoceptor antagonist, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Bush et al. by substituting the human β_3-

adrenoceptor agonist SAM II with the human β_3-adrenoceptor agonist BRL 37344, as taught by Moniotte et al., and to co-administer a human β_1-/β_2-adrenoceptor antagonist such as nadolol, as taught by the ESC Guidelines, with a reasonable expectation of success.

As recognized by MPEP §2144.06, “it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

RESPONSE TO ARGUMENTS

Applicant's amendments and arguments filed 11/30/2010 have been fully considered but they are not persuasive.

The patient population recited by the newly amended claims is "a human suffering from chronic symptomatic heart failure with impaired systolic left ventricular function.” However, this limitation does not meaningfully distinguish the claimed patient population from the patient population disclosed in the prior art.

Specifically, the instant specification (p. 1, line 24) and MedLinePlus (para. 1; cited in the previous Action) use the terms "heart failure" and "congestive heart failure" (CHF) interchangeably. As evidenced by the ESC Guidelines (cited in the previous Action), “[m]any additional words or phrases are used to characterize patients with heart

failure (HF). These terms can overlap and physicians do sometimes use words with a slightly different meaning" (p. 936, left col.).

The ESC Guidelines define heart failure as a clinical syndrome with three components: *symptoms* typical of heart failure, *signs* typical of heart failure, and *objective evidence* of a structural or functional abnormality of the heart at rest (Table 3). Thus, heart failure as a clinical syndrome is by definition symptomatic.

Further, chronic heart failure is "by far the most common form of HF leading to hospital admission, accounting for 80% of cases" (p. 936, right col.).

The ESC Guidelines recognize that a distinction is frequently made between systolic and diastolic HF, but observe that the distinction is somewhat arbitrary. Diastolic HF is characterized by a left ventricular ejection fraction (LVEF) above 40-50%, while a LVEF below about 40% is considered systolic HF. However, since both systolic and diastolic HF encompass impaired left ventricular function, "most patients with HF have evidence of both systolic and diastolic dysfunction at rest or on exercise. Diastolic and systolic HFs should not be considered as separate entities" (p. 936, right col.).

Thus, by disclosing the administration of a β_3 adrenoceptor agonist to humans to treat, *inter alia*, congestive heart failure (p. 25), Bush et al. disclose the administration of a β_3 adrenoceptor agonist to substantially the same patient population as that claimed, i.e., humans suffering from chronic symptomatic heart failure with impaired systolic left ventricular function.

Applicant contends that "the Bush reference cannot bear the weight the examiner puts on it" (Remarks, p. 15). In particular, Applicant contends that Bush et al. disclose

the β_3 adrenoceptor agonist (SAM II), developed for the treatment of obesity and/or diabetes, in the treatment of "seemingly random conditions;" and that Bush et al. disclose only two functional examples which do not support the administration of a β_3 adrenoceptor agonist to treat heart failure with any expectation of success.

However, Bush et al. disclose each and every claim limitation within the four corners of the reference, which is effective as prior art for all it discloses. As recognized by MPEP §2121, prior art is presumed to be enabling; "proof of efficacy is not required for a prior art reference to be enabling for purposes of anticipation." *Impax Labs. Inc. v. Aventis Pharm. Inc.,* 468 F.3d 1366, 1383, 81 USPQ2d 1001, 1013 (Fed. Cir. 2006).

In addition, MPEP § 2123 (II) recognizes that nonpreferred and alternative embodiments constitute prior art. "Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments." *In re Susi,* 440 F.2d 442, 169 USPQ 423 (CCPA 1971).

Further, Applicant contends that Moniotte et al. provide no data or references to support their speculations; that a skilled practitioner would have placed no credence on these unsubstantiated speculations (Remarks, p. 12); and that the disclosure of Moniotte et al. would have been regarded as too simplistic to have any credibility amongst practitioners skilled in the art (Remarks, p. 13).

These assertions appear to be directed to the factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), in particular the third "Graham factor," resolving the level of ordinary skill in the pertinent art. However, Applicant's assertions are not supported by the current record. Moniotte et al. held

positions at the Department of Internal Medicine at the University of Louvain Medical School in Brussels, Belgium. Thus, absent evidence to the contrary, it is unclear why persons having ordinary skill in the art would have had reason to dismiss the reference as "too simplistic" or as "unsubstantiated speculation."

As recognized by MPEP § 716.01(c)(II), attorney arguments cannot take the place of evidence. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Because the Graham factors are factual inquiries, these assertions must be supported by factual evidence, such as an appropriate affidavit or declaration.

For the forgoing reasons, the rejection of claims 3 and 5 under 35 U.S.C. §102(b) as anticipated by Bush et al., and the rejection of claims 3 and 5-12 under 35 U.S.C. §103 as obvious over Bush et al. in view of Moniotte et al. and ESC Guidelines, are maintained.

Allowable Subject Matter

Claims 13 and 14 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

CONCLUSION

Claims 3 and 5-12 are rejected.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARA E. TOWNSLEY whose telephone number is (571) 270-7672. The examiner can normally be reached on Mon - Fri, 9:30 am - 6:00 pm (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian-Yong Kwon, can be reached at 571-272-0581. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SARA E. TOWNSLEY/
Examiner, Art Unit 1613

/BARBARA P. BADIO/
Primary Examiner, Art Unit 1628